MODIFIED FORM PTO-1083

Atty. Dkt. No. 46403-1009

Date: May 16, 2001

UTILITY PATENT APPLICATION TRANSMITTAL and FEE TRANSMITTAL

Inventor(s) : Yajun GUO
Serial No. : 09/216,062
Filed : December 18, 1998
For : CELLULAR VACCINES AND IMMUNOTHERAPEUTICS AND METHODS FOR THEIR PREPARATION

COMMISSIONER FOR PATENTS
Washington, D.C. 20231

Sir:

Transmitted herewith is:

X Supplemental Response to Advisory Action mailed March 13, 2001
__ Petition for Extension of Time (__ months)
X Check in the amount of $396.00
X Copy of Declaration of Jing Ma and Yajun Guo
X Postcard

The fee has been calculated as shown below:

	(Col. 1) CLAIMS REMAINING AFTER AMENDMENT		(Col. 2) HIGHEST NO. PREVIOUSLY PAID FOR	(Col. 3) PRESENT EXTRA	SMALL ENTITY RATE	FEE		OTHER THAN A SMALL ENTITY RATE	FEE
TOTAL CLAIMS	66	-	22*	= 44*	× $ 9	$396.00	OR	× $ 18	$0
INDEP CLAIMS	2	-	3***	= 0*	× $ 40	$	OR	× $ 80	$0.00
___ PRESENTATION OF MULTIPLE DEP. CLAIM					+ $135	$	OR	+ $270	$0
					TOTAL	$396.00	OR	TOTAL	$0.00

* If the entry in Col. 1 is less than the entry in Col. 2. write "0" in Col. 3.
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, write "20" in this space.
*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, write "3" in this space. The "Highest Number Previously Paid For" (Total or Independent) is the highest number found from the equivalent box on Col. 1 of a prior amendment or the number of claims originally filed.

__ Please charge my Deposit Account No. 02-0410 the amount of $0.00. A duplicate copy of this transmittal letter is enclosed.

X The Commissioner is hereby authorized to charge payment of the following fees associated with this communication or credit any overpayment to Deposit Account No. 02-0410 (Baker & McKenzie). A duplicate copy of this transmittal letter is enclosed.
X Any filing fees under 37 CFR 1.16.
X Any patent application processing fees under 37 CFR 1.17.

Respectfully submitted,

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CERTIFICATE OF MAILING

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Signature: Karen M. Cruz

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Atty. Dkt. No. R460/2000

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: YAJUN GUO	)	Group Art Unit:	1644
	)		
	)	Examiner:	Dibrino, M.
Serial No.: 09/216,062	)		
	)		
Filed: December 18, 1998	)		
	)		
For: CELLULAR VACCINES AND IMMUNOTHERAPEUTICS AND METHODS FOR THEIR PREPARATION	)		

San Diego, California 92101
May 16, 2001

Commissioner for Patents
Washington, D.C. 20231

SUPPLEMENTAL RESPONSE

Dear Sir:

Further to the response file March 13, 2001, please enter the following amendments and consider the following remarks.

05/22/2001 AGOITOM 00000062 09216062
01 FC:203 396.00 OP

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Signature: KMC
Karen M. Cruz

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AMENDMENTS

Please cancel claims 1-4, 6 and 23-44 without prejudice and add new claims 45-110 as follows:

--45. A method of preparing a pharmaceutical composition or therapeutic vaccine, said method comprising the steps of:

(a) providing a plurality of hepatocellular carcinoma cells, lymphoma cells, colon carcinoma cells or gastric cancer cells;

(b) treating said hepatocellular carcinoma cells, lymphoma cells, colon carcinoma cells or gastric cancer cells to increase the levels of CD28, 4-1BB, or CTLA-4 molecules in said cells;

(c) providing a plurality of a bispecific monoclonal antibodies, each of said antibodies comprising a binding site for a CD28, 4-1BB or CTLA-4 molecule on the surface of T cells in a patient mammal and a binding site for a gp55, gp95, gp115 or gp210 antigen;

(d) attaching said bispecific monoclonal antibodies to said cells; and

(e) thereafter collecting a pharmaceutically effective amount of said cells with said bispecific monoclonal antibodies attached thereto; wherein said steps (c) and (d) are performed either before or after said step (b).

46. The method of claim 45, wherein said one or more hepatocellular carcinoma cells, lymphoma cells, colon carcinoma cells or gastric cancer cells comprise one or more hepatocellular carcinoma cells.

47. The method of claim 45, wherein said one or more hepatocellular carcinoma cells, lymphoma cells, colon carcinoma cells or gastric cancer cells comprise one or more lymphoma cells.

48. The method of claim 45, wherein said one or more hepatocellular carcinoma cells, lymphoma cells, colon carcinoma cells or gastric cancer cells comprise one or more colon carcinoma cells.

49. The method of claim 45, wherein said one or more hepatocellular carcinoma cells, lymphoma cells, colon carcinoma cells or gastric cancer cells comprise one or more gastric cancer cells.

50. The method of claim 45, wherein said CD28, 4-1BB or CTLA-4 molecule comprises a CD28 molecule.

51. The method of claim 45, wherein said CD28, 4-1BB or CTLA-4 molecule comprises one or more 4-1BB molecules.

52. The method of claim 45, wherein said CD28, 4-1BB or CTLA-4 molecule comprises one or more CTLA-4 molecules.

53. The method of claim 45, wherein said patient mammal is a human.

54. The method of claim 45, wherein the one or more hepatocellular carcinoma cells, lymphoma cells, colon carcinoma cells or gastric cancer cells are treated with IFN-γ.

55. The method of claim 45, wherein the one or more hepatocellular carcinoma cells, lymphoma cells, colon carcinoma cells or gastric cancer cells are treated with TNF-α.

56. The method of claim 45, wherein the one or more hepatocellular carcinoma cells, lymphoma cells, colon carcinoma cells or gastric cancer cells are treated with IFN-γ and TNF-α.

57. The method of claim 45, wherein said T cells are CD3+CD8+CD25+ T cells.

58. The method of claim 45, wherein said antibodies comprise two or more antigen binding sites for gp55, gp95, gp115, or gp210 antigens on the surface of said one or more hepatocellular carcinoma cells, lymphoma cells colon carcinoma cells or gastric cancer cells.

59. The method of claim 45, wherein said antibodies comprise two or more binding sites for said CD28, 4-1BB or CTLA-4 molecules on the surface of T cells in said patient mammal.

60. The method of claim 45, wherein said hepatocellular carcinoma cells, lymphoma cells, colon carcinoma cells or gastric cancer cells are treated with 10-100 U of IFN-γ and 10-100 U of TNF-α.

61. The method of claim 45, wherein said hepatocellular carcinoma cells, lymphoma cells, colon carcinoma cells or gastric cancer cells are treated with 100 U of IFN-γ and 50 U of TNF-α.

62. The method of claim 46, where said hepatocellular carcinoma cells are hepa 1-6 cells.

63. The method of claim 47, wherein said lymphoma cells are EL-4 cells.

64. The method of claim 48, wherein said colon carcinoma cells are SMCC-1 cells.

65. The method of claim 45, wherein said one or more gp55, gp95, gp115, or gp210 antigens comprise gp55 antigens.

66. The method of claim 45, wherein said one or more gp55, gp95, gp115, or gp210 antigens comprise gp95 antigens.

67. The method of claim 45, wherein said one or more gp55, gp95, gp115, or gp210 antigens comprise gp115 antigens.

68. The method of claim 45, wherein said one or more gp55, gp95, gp115, or gp210 antigens comprise gp210 antigens.

69. The method of claim 45, wherein said collecting in step (e) comprises the step of removing said bispecific monoclonal antibodies not attached to said cells.

70. An immunogenic composition, comprising:

a pharmaceutically effective amount of one or more isolated autologous hepatocellular carcinoma cells, lymphoma cells, colon carcinoma cells or gastric cancer cells which express one or more CD28, 4-1BB, or CTLA-4 molecules at a level higher than in said cells in a patient mammal; and

a pharmaceutically effective amount of one or more bispecific monoclonal antibodies comprising a binding site for a CD28, 4-1BB or CTLA-4 molecule on the surface of T cells in a patient mammal, and a binding site for a gp55, gp95, gp115, or gp210 antigen, wherein said bispecific monoclonal antibodies are attached to said cells, and wherein said composition is substantially free of bispecific monoclonal antibodies not attached to said cells.

71. The composition of claim 70, wherein said composition is isolated.

72. The composition of claim 70, wherein said composition is enriched.

73. The composition of claim 70, wherein said composition is purified.

74. The composition of claim 70, wherein said one or more hepatocellular carcinoma cells, lymphoma cells, colon carcinoma cells or gastric cancer cells comprise one or more hepatocellular carcinoma cells.

75. The composition of claim 70, wherein said one or more hepatocellular carcinoma cells, lymphoma cells, colon carcinoma cells or gastric cancer cells comprise one or more lymphoma cells.

76. The composition of claim 70, wherein said one or more hepatocellular carcinoma cells, lymphoma cells, colon carcinoma cells or gastric cancer cells comprise one or more colon carcinoma cells.

77. The composition of claim 70, wherein said one or more hepatocellular carcinoma cells, lymphoma cells, colon carcinoma cells or gastric cancer cells comprise one or more gastric cancer cells.

78. The composition of claim 70, wherein said CD28, 4-1BB or CTLA-4 molecule comprises one or more CD28 molecules.

79. The composition of claim 70, wherein said CD28, 4-1BB or CTLA-4 molecule comprises one or more 4-1BB molecules.

80. The composition of claim 70, wherein said CD28, 4-1BB or CTLA-4 molecule comprises one or more CTLA-4 molecules.

81. The composition of claim 70, wherein said patient mammal is a human.

82. The composition of claim 70, wherein the one or more hepatocellular carcinoma, lymphoma, colon carcinoma cells or gastric cancer cells are treated with IFN-γ.

83. The composition of claim 70, wherein the one or more hepatocellular carcinoma cells, lymphoma cells, colon carcinoma cells or gastric cancer cells are treated with TNF-α.

84. The composition of claim 70, wherein the one or more hepatocellular carcinoma cells, lymphoma cells, colon carcinoma cells or gastric cancer cells are treated with IFN-γ and TNF-α.

85. The composition of claim 70, wherein said T cells are CD3+CD8+CD25+ T cells.

86. The composition of claim 70, further comprising a pharmaceutically acceptable carrier or excipient.

87. The composition of claim 70, wherein said antibodies comprise two or more antigen binding sites for gp55, gp95, gp115, or gp210 antigens on the surface of said one or more hepatocellular carcinoma cells, colon carcinoma cells or gastric cancer cells.

88. The composition of claim 70, wherein said antibodies comprise two or more binding sites for said CD28, 4-1BB or CTLA-4 molecule on the surface of T cells in said patient mammal.

89. The composition of claim 70, wherein said composition comprises two or more antibodies comprising an antigen binding site for a gp55, gp95, gp115, or gp210 antigen on the surface of said one or more hepatocellular carcinoma cells, lymphoma cells, colon carcinoma cells or gastric cancer cells.

90. The composition of claim 70, wherein said composition comprises two or more antibodies each comprising a binding site for a different one of said CD28, 4-1BB or CTLA-4 molecules.

91. The composition of claim 70, wherein said composition comprises two or more antibodies each attached to a different antigen.

92. The composition of claim 70, further comprising a pharmaceutically effective amount of IFN-γ, TNF-α, or both.

93. The composition of claim 70, wherein said hepatocellular carcinoma cells, lymphoma, colon carcinoma cells or gastric cancer cells are treated with 10-100 U of IFN-γ and 10-100 U of TNF-α.

94. The composition of claim 70, wherein said hepatocellular carcinoma cells, lymphoma, colon carcinoma cells or gastric cancer cells are treated with 100 U of IFN-γ and 50 U of TNF-α.

95. The composition of claim 74, where said hepatocellular carcinoma cells are hepa 1-6 cells.

96. The composition of claim 75, wherein said lymphoma cells are EL-4 cells.

97. The composition of claim 76, wherein said colon carcinoma cells are SMCC-1 cells.

98. The composition of claim 70, wherein said gp55, gp95, gp115, or gp210 antigen comprises gp55 antigens.

99. The composition of claim 70, wherein said gp55, gp95, gp115, or gp210 antigen comprises gp95 antigens.

100. The composition of claim 70, wherein said gp55, gp95, gp115, or gp210 antigen comprises gp115 antigens.

101. The composition of claim 70, wherein said gp55, gp95, gp115, or gp210 antigen comprises gp210 antigens.

102. The composition of claim 70, wherein said one or more hepatocellular carcinoma cells, lymphoma cells, colon carcinoma cells or gastric cancer cells express said CD28, 4-1BB or CTLA-4 molecule at a level 50% higher than the amount that said CD28, 4-1BB or CTLA-4 molecule is expressed from hepatocellular carcinoma cells, lymphoma cells, colon carcinoma cells or gastric cancer cells in a patient mammal.

103. The composition of claim 70, wherein said hepatocellular carcinoma cells, lymphoma cells, colon carcinoma cells or gastric cancer cells expresses said CD28, 4-1BB or CTLA-4 molecule at a level 2 fold higher than the amount that said CD28, 4-1BB or CTLA-4 molecule is expressed hepatocellular carcinoma cells, lymphoma cells, colon carcinoma cells or gastric cancer cells in a patient mammal.

104. The composition of claim 70, wherein said hepatocellular carcinoma cells, lymphoma cells, colon carcinoma cells or gastric cancer cells expresses said CD28, 4-1BB or CTLA-4 molecule at a level 10 fold higher than the amount that said CD28, 4-1BB or CTLA-4

molecule is expressed from hepatocellular carcinoma cells, lymphoma cells, colon carcinoma cells or gastric cancer cells in a patient mammal.

105. The composition of claim 70, wherein substantially all of said antibodies are attached to said hepatocellular carcinoma cells, lymphoma cells, colon carcinoma cells or gastric cancer cells.

106. The composition of claim 70, wherein over 80% of said antibodies are attached to said hepatocellular carcinoma cells, lymphoma cells, colon carcinoma cells or gastric cancer cells.

107. The composition of claim 70, wherein over 90% of said antibodies are attached to said hepatocellular carcinoma cells, lymphoma cells, colon carcinoma cells or gastric cancer cells.

108. The composition of claim 70, wherein over 95% of said antibodies are attached to said hepatocellular carcinoma cells, lymphoma cells, colon carcinoma cells or gastric cancer cells.

109. The composition of claim 70, wherein the composition is substantially free of said antibodies that are not bound to said hepatocellular carcinoma cells, lymphoma cells, colon carcinoma cells or gastric cancer cells.

110. The composition of claim 70, wherein a pharmaceutically effective amount of said antibodies are bound to said hepatocellular carcinoma cells, lymphoma cells, colon carcinoma cells or gastric cancer cells.--.